10/16/03

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October 8, 2003

By Michelle Chan

PATENT
100/07010

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:
CLAUDIA B. JAFFE
Application No.: 09/696,749
Filed: October 24, 2000
For: Pressure Induced Reagent Introduction and Electrophoretic Separation

Examiner: Jennine M. Brown

Art Unit: 1755

DECLARATION UNDER 37 C.F.R. § 1.131

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

I, Claudia B. Jaffe, declare as follows:

1. I am the inventor of the invention claimed in the above-referenced application, as amended by the Response filed on February 18, 2003.
2. I conceived and reduced to practice the invention claimed in claim 1 of the above-referenced application before April 16, 1999.
    a. Before April 16, 1999, I submitted Invention Disclosure Form No. 98-078. Note that at that time my name was Claudia B. Cohen. A true and correct copy of Invention Disclosure Form No. 98-078, in which the dates have been redacted, is attached hereto. The submitted invention disclosure included the graphical data on the last page.
    b. The invention documented in Invention Disclosure Form No. 98-078 provides a description of the invention covered in claim 1 of the above-referenced application. Specifically, the Form describes a microfluidic device comprising a mixing channel and a separation channel in which the mixing channel has a larger cross-sectional area than the separation channel; a pressure source to introduce one or more samples into the mixing channel; and an electrokinetic controller to

transport sample into the separation channel by the application of a voltage to the separation channel.

c. Invention Disclosure Form No. 98-078 also demonstrates my reduction to practice of the invention covered in claim 1 of the above-referenced application. The data attached to the Form show the results of a separation carried out on a microfluidic device in accordance with claim 1 of the above-reference application. This device comprised a mixing channel and a separation channel with a smaller cross sectional area than the mixing channel. Within this device, pressure was used to move a sample into the mixing channel, and then a voltage was applied across the separation channel to move sample into the separation channel.

3. I further declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

October 4 2003
Date

Claudia B. Jaffe

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CONFIDENTIAL
CALIPER TECHNOLOGIES CORP.
INVENTION DISCLOSURE FORM

This Invention Disclosure form is intended to provide a common format for the rapid and convenient submission of invention disclosures for consideration and/or filing of patent applications. Please provide as much of the requested information as possible. Use additional sheets as necessary.

Disclosure No.:
Docketed:
Considered on:
[Patent Committee Use Only]

I. GENERAL INFORMATION

Name and ext. of person submitting disclosure: **Claudia B. Cohen**

Date submitted:

Brief statement of the invention:

Coupling pressure-induced flow with electrophoretic separations requires a double depth chip design. The wider, deeper channel for the reagent introduction and sample mixing is necessary for low resistance to fluid flow. However, a shallower channel must be used for the separation. Because the resistance to flow goes as one over the channel height cubed, a shallow channel prevents parabolic flow from contributing significantly to the flux in the separation channel. In addition, the shallow channel dimensions dictate the amount of reagent injected into the separation channel. In instances where pressure-induced flow in one part of the labchip is coupled to a separation channel or channels, the shallow channel dimensions are necessary to get an efficient, highly resolved separation and baseline resolved peaks. Minimizing injection time, regulating pinching currents and manipulating reagent concentrations is not always sufficient to prevent sample loading. Two regimes of channel dimensions are necessary to uncouple the mechanisms of the flow in different channels in the labchip and to obtain clean separations.

Name(s) and ext.: of other individual(s) who assisted in the development of the invention:

II. PRIOR OR EXPECTED DISCLOSURE OF THE INVENTION

To the best of your knowledge, has the invention been: (1) discussed with any potential purchasers; (2) sold or offered for sale; (3) employed commercially (if the invention is a process); (4) described in a printed publication; (5) disclosed in a talk or otherwise presented at a public meeting; (6) otherwise disclosed to vendors or customers; or (7) is any future disclosure currently anticipated? **NO**

If the answer to any of these questions is "yes," please provide additional details, including dates of publication or disclosure or expected publication or disclosure:

_____

_____

III. CALIPER'S RIGHTS TO THE INVENTION

To the best of your knowledge: (1) is there any agreement between Caliper and another entity (person, institution or corporation) that deals with the rights to or ownership of this invention; (2) is the invention the result of a collaboration with someone who is not a Caliper employee? **NO**

If the answer to either of these questions is "yes," please provide details, including the names of the persons, corporations or institutions:

_____

_____

IV. DESCRIPTION OF THE INVENTION

A. Please provide a brief description of the invention sufficient to convey the general ideas covered (1-4 paragraphs). You may also attach notebook pages, computer printouts, etc., if they are sufficient to convey the ideas of the invention.

Methods for controlling sample loading in a separation done on a single depth chip of standard dimension consist of manipulating the timing of the injection, the degree of pinching current and concentrations used in the reaction channel. Despite the number of degrees of freedom these methods offer it is often not possible to get baseline-resolved separations in reactions done on planar chips. Longer channels allow for improved resolution. However, channel length on the labchip is restricted by the limited chip area and defined locations for reagent and waste wells.

An alternative for control of load volume is channel dimension. As an example, a cross injector for separations in a standard channel of dimension 70 um wide x 20 um deep contains 400 times the volume of a shallow, narrow channel of dimension 9 um wide x 3 um deep. When coupling pressure driven flow with separations based assays, the shallow channels allow for the uncoupling of parabolic flow and electroosmotic flow and offer a regime of channel dimensions the allows for good separations.

B. What aspects of the invention can be readily varied or altered and yet still accomplish the objective of the invention?

It is possible to fabricate mixing channels of a broad range of dimension for facilitating pressure-induced flow. These mixing channels can cross the separation channel directly or first feed into a loading channel that intersects a separation channel. If the loading and separation channels are both narrow and shallow the most discrete volumes of samples can be injected. As little as 1um deep and 5 um wide channels have been fabricated to date.

C. Are you aware of any other systems (similar or otherwise) which address the same problems? If yes, please provide details (e.g., literature or patent citation, if available).

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D. Please provide cross-references (if any) to a notebook or other data archive.

Attached separation on 668 chip @ 9X3um channels

Notebook 119 / cac119-178.xls

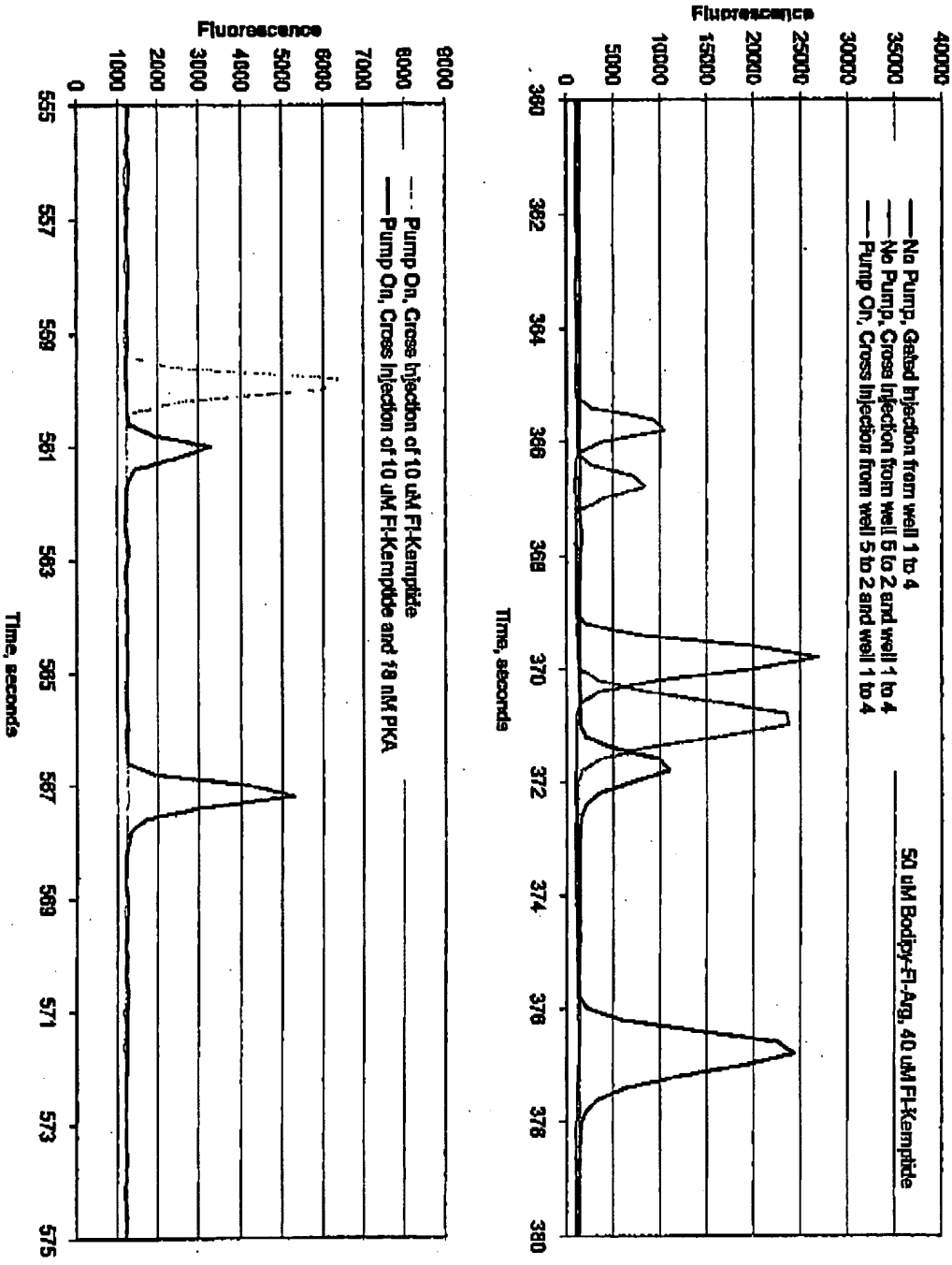
RECEIVED
CENTRAL FAX CENTER
OCT 0 9 2003
OFFICIAL

V. SIGNATURE

Name: Claudia B. Chen

Signature: [signature]

Date: ____________


Pressure Driven Introduction of Reagents onto 66B Chip,
Electrophoretic Separation During Pumping
Fluorescence
Time, seconds
No Pump, Gated Injection from well 1 to 4
No Pump, Cross Injection from well 5 to 2 and well 1 to 4
Pump On, Cross Injection from well 5 to 2 and well 1 to 4
50 uM Bodipy-Fl-Arg, 40 uM Fl-Kemptide
Fluorescence
Time, seconds
Pump On, Cross Injection of 10 uM Fl-Kemptide
Pump On, Cross Injection of 10 uM Fl-Kemptide and 18 nM PKA
100 mM HEPES, pH 7.5, 1 M NDSB-195, 5 mM MgCl2, 100 uM ATP, 10 mM DTT, 0.1% TritonX-100